

**CLAIMS**

No amendments are requested. The status of the claims is as follows:

1. - 39. (Canceled)

40. (Previously presented) A microfabricated device for fragmenting nucleic acids present in a fluid sample, the device comprising an inlet port, a fragmentation cell, and an outlet port downstream from said inlet port, said cell being in fluid communication with said ports, and wherein said outlet port is dimensioned to impede the flow of a fluid sample out of said cell so as to effect shearing of nucleic acids molecules therein, wherein the fragmentation cell comprises a chamber having a bottom wall in which is formed the outlet port, the bottom wall being generally perpendicular to the direction of flow of fluid through the outlet port, and wherein the fragmentation cell has a top wall in which the inlet port is formed, and side walls which extend from the top wall to the bottom wall, and wherein the side walls taper inwardly to meet the inlet port.

41. (Previously presented) A microfabricated device as claimed in claim 40, wherein the fragmentation cell has the shape of an irregular polygon, preferably an irregular hexagon, with an essentially straight bottom wall in which the outlet port is formed at approximately the mid point, and wherein the bottom wall is substantially perpendicular to the longitudinal axis of the outlet port.

42. (Previously presented) A microfabricated device as claimed in claim 40, wherein the fragmentation cell is generally pear shaped with an essentially straight bottom wall in which the

outlet port is formed at approximately the mid point, the bottom wall being substantially perpendicular to the longitudinal axis of the outlet, and wherein the bottom wall is connected by curved walls to side walls, which converge or taper inwardly to meet the inlet port.

43. (Previously presented) A microfabricated device as claimed in claim 40, wherein the width of the fragmentation cell abruptly decreases at the outlet port.

44. (Previously presented) A microfabricated device as claimed in claim 40, wherein the outlet port comprises a constriction having a width in the range of from 1 to 100  $\mu\text{m}$ .

45. (Previously presented) A microfabricated device as claimed in claim 40, wherein the outlet port is formed in approximately the middle of the bottom wall.

46. (Previously presented) A microfabricated device as claimed in claim 40, wherein the side walls taper inwardly to meet the outlet port.

47. (Previously presented) A microfabricated device as claimed in claim 40, wherein the bottom wall is adjacent and substantially perpendicular to two lower side wall portions.

48. (Previously presented) A microfabricated device as claimed in claim 47, wherein the upper portions of the side walls taper inwardly to meet the inlet port.

49. (Previously presented) A microfabricated device as claimed in claim 40, wherein side walls or portions thereof next to or adjacent the inlet port subtend an angle of less than 90 degrees to the longitudinal axis of the inlet port.

50. (Previously presented) A microfabricated device as claimed in claim 40, wherein the fragmentation cell comprises a bottom wall in which the outlet port is formed at approximately the mid point, the bottom wall being substantially perpendicular to the longitudinal axis of the outlet, and side walls which converge or taper inwardly to meet the inlet port.

51. (Previously presented) A microfabricated device as claimed in claim 40, wherein the device further comprises an obstacle located in the cell in the direct path between the inlet and outlet ports.

52. (Previously presented) A microfabricated device as claimed in claim 51, wherein the space between sides of the obstacle and sides of the cell defines a bifurcated path for the fluid sample.

53. (Previously presented) A microfabricated device as claimed in claim 51, wherein the obstacle is shaped so that the flow path of a fluid sample in a region adjacent the outlet port is substantially perpendicular to the longitudinal axis of the outlet.

54. (Previously presented) A microfabricated device as claimed in claim 51, wherein the obstacle is in the form of a generally triangular obstacle, with its three sides substantially parallel to the bottom wall and side walls of the cell, the space between the sides of the obstacle and the sides of the cell defining a bifurcated path for the fluid sample.

55. (Previously presented) A microfabricated device as claimed in claim 40, wherein the fragmentation cell is asymmetric about the horizontal axis and substantially symmetric about the

longitudinal axis, the longitudinal axis being essentially coincident with the direction of flow.

56. (Previously presented) A microfabricated device as claimed in claim 40, further comprising an access channel in fluid communication with the inlet port.

57. (Previously presented) A microfabricated device as claimed in claim 40, further comprising collection means in fluid communication with the outlet port.

58. (Previously presented) A microfabricated device as claimed in claim 40, further comprising means for effecting flow of a sample into the inlet port, through the fragmentation cell and out of the outlet port.

59. (Previously presented) A microfabricated device as claimed in claim 58, wherein said means for effecting flow comprises one or more pumps.

60. (Previously presented) A microfabricated device as claimed in claim 58, wherein said means for effecting flow comprises one or more variable volume chambers in communication with the inlet port and/or outlet port, wherein altering the volume of the variable volume chamber(s) effects and/or restricts flow of a fluid sample into and/or out of the fragmentation cell.

61. (Previously presented) A microfabricated device as claimed in claim 40 which comprises a substrate and an overlying cover, the fragmentation cell being defined by a recess in a surface of the substrate and the adjacent surface of the cover.

62. (Previously presented) A microfabricated device as claimed in claim 61, wherein the substrate is formed from silicon

and the overlying cover from glass.

63. (Previously presented) A microfabricated device as claimed in claim 62, wherein the glass cover is anodically bonded to the silicon substrate.

64. (Previously presented) A microfabricated device as claimed in claim 40 which comprises at least first and second fragmentation cells, the outlet port of the first cell being in fluid communication with the inlet port of the second cell.

65. (Previously presented) A microfabricated device as claimed in claim 64, further comprising a third fragmentation cell, the outlet port of the second cell being in fluid communication with the inlet port of the third cell.

66. (Previously presented) A microfabricated device as claimed in claim 64 comprising a plurality of serially connected fragmentation cells.

67. (Previously presented) A microfabricated device as claimed in claim 64, wherein the size of the outlet port decreases the further down stream the fragmentation cell.

68. (Previously presented) A microfabricated device as claimed in claim 67, wherein the size of the outlet port gradually decreases from the first fragmentation cell to the last fragmentation cell downstream.

69. (Previously presented) A microfabricated device as claimed in claim 40 for fragmenting nucleic acids present in a biological fluid, a dairy product, an environmental fluid or drinking water.

70. (Previously presented) A microfabricated reaction chamber system for carrying out a nucleic acid sequence amplification and detection process on a nucleic acid sample, the system comprising a microfabricated device as defined in claim 40.

71. (Previously presented) An apparatus for the analysis of biological and/or environmental samples, the apparatus comprising a device as defined in claim 40.

72. (Previously presented) An assay kit for the analysis of biological and/or environmental samples, the kit comprising a device as defined in claim 40 and means for contacting the sample with the device.

73. (Previously presented) An apparatus as claimed in claim 71 which is disposable.

74. (Previously presented) A process for fragmenting nucleic acids present in a fluid sample, the process comprising:

- (a) providing a device as defined in claim 40;
- (b) providing a fluid sample comprising nucleic acids;
- (c) pumping the fluid sample into the inlet port of said device, through the fragmentation cell and out of the outlet port; and
- (d) collecting the thus fragmented sample at the outlet port.

75. (Previously presented) A process as claimed in claim 74 which further involves a nucleic acid sequence amplification and detection process on the fragmented nucleic acid sample.

76. (Previously presented) The microfabricated device as claimed in claim 62, wherein the glass cover is anodically bonded

to the silicon substrate optionally through an intermediate silicon oxide layer formed on the surface of the substrate.

77. (Previously presented) The microfabricated device as claimed in claim 44 wherein the constriction width is from 5 to 50  $\mu\text{m}$ .